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# The Psychological Burden of Skin Diseases: A Cross-Sectional Multicenter Study among Dermatological Out-Patients in 13 European Countries

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The contribution of psychological disorders to the burden of skin disease has been poorly explored, and this is a large-scale study to ascertain the association between depression, anxiety, and suicidal ideation with various dermatological diagnoses. This international multicenter observational cross-sectional study was conducted in 13 European countries. In each dermatology clinic, 250 consecutive adult out-patients were recruited to complete a questionnaire, reporting socio-demographic information, negative life events, and suicidal ideation; depression and anxiety were assessed with the Hospital Anxiety and Depression Scale. A clinical examination was performed. A control group was recruited among hospital employees. There were 4,994 participants—3,635 patients and 1,359 controls. Clinical depression was present in 10.1% patients (controls 4.3%, odds ratio (OR) 2.40 (1.67–3.47)). Clinical anxiety was present in 17.2% (controls 11.1%, OR 2.18 (1.68–2.82)). Suicidal ideation was reported by 12.7% of all patients (controls 8.3%, OR 1.94 (1.33–2.82)). For individual diagnoses, only patients with psoriasis had significant association with suicidal ideation. The association with depression and anxiety was highest for patients with psoriasis, atopic dermatitis, hand eczema, and leg ulcers. These results identify a major additional burden of skin disease and have important clinical implications.

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## INTRODUCTION

Despite the high prevalence of skin conditions (Rea *et al.*, 1976; Dalgard *et al.*, 2004) and the strong association of psychiatric disorders with skin disease (Hughes *et al.*, 1983, Picardi *et al.*, 2000), the true extent of psychological co-morbidity across Europe is not known. This is important because the care of patients with skin disease may be inadequate if their psychological problems are not also recognized and treated.

The Global Burden of Diseases Study recently demonstrated that skin diseases were the fourth leading cause of nonfatal disease burden (Hay *et al.*, 2014). Assessing the burden of skin disease is crucial for evidence-based allocation of resources and to position Dermatology in a global health perspective

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*Work done in Giessen, Germany and Oslo, Norway. Patient recruitment in dermatological out-patient clinics from 13 European countries*

*Abbreviations: CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; OR, odds ratio*

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(Freeman, 2014), but the choice of appropriate method remains a challenge. A wider perspective of the burden of physical conditions is demonstrated by the significant occurrence of depression in diabetes, asthma, heart disease, and arthritis (Scott *et al.*, 2007). It is predicted that depressive disorder will be the second cause of disease burden worldwide by 2030 (Mathers and Loncar, 2006), and the contribution of mental health to the burden of physical conditions is stressed in the context of the World Health Organization strategies by their slogan ''there is no health without mental health'' (Prince *et al.*, 2007). The co-occurrence of mood disorders and physical conditions has been emphasized by the World Mental Health Survey (Scott *et al.*, 2007, 2010). Measurement of the mental health of patients with physical diseases may therefore appropriately contribute to the overall measurement of the burden of disease.

European studies have shown that patients with atopic eczema, hand eczema, acne, and hidradenitis suppurativa have an increased risk of depression (Cvetkovski *et al.*, 2006; Dalgard *et al.*, 2008; Onderdijk *et al.*, 2013; Sanna *et al.*, 2014a), and 10% of patients with psoriasis are clinically depressed (Dowlatshahi *et al.*, 2013). Although anxiety is a separate entity, it is less studied and mostly described as accompanying depression in dermatological patients with psoriasis and occupational eczema (Boehm *et al.*, 2012; Kurd *et al.*, 2010). Population-based studies have shown significant associations of acne, eczema, and psoriasis with suicidal thoughts (Kurd *et al.*, 2010; Halvorsen *et al.*, 2011, 2014). In a study from Germany, 16% of patients with atopic dermatitis had suicidal ideation compared with 1% of the controls (Dieris-Hirche *et al.*, 2009).

Little is known about psychological co-morbidity of common skin diseases from a global perspective. The aim of this study was to investigate the co-occurrence of depression, anxiety, and suicidal thoughts in patients with common skin diseases across several European countries.

## RESULTS

In total, 5,067 individuals agreed to take part—3,651 patients and 1,416 controls. The participation rate was 79.9%. Of the initial 3,651 patients, 16 were excluded, 9 because they were too young and 6 because of missing data, leaving 3,635. Of the initial 1,416 controls, 57 were excluded because they had a skin disease, leaving 1,359 (see flow chart).

The subject characteristics are given in Table 1: there were more females in both the patient and control populations. The mean patient age was 47 years versus 41 years for the controls, $P<0.001$. Overall 92% participants originated from the country where the study took place (data not shown). The socio-economic level distribution was similar in the two groups. Overall 35.6% of the patients reported stress compared with 30.6% of the controls, $P<0.001$. Overall patients had more physical co-morbidities compared with the controls, 28.8% versus 16.0%, $P<0.001$.

The overall distribution of the skin conditions is given in Table 2. The most common skin conditions were as follows: psoriasis (17.4%), non-melanoma skin cancer (10.9%), infections of the skin (6.8%), eczema (6.4%), acne (5.9%), nevi (4.9%), atopic eczema (4.5%), skin tumors (4.2%), hand eczema (4.0%), and leg ulcers (3.4%).

Data on depression among dermatological patients are given in Table 3. Overall 10.1% dermatological patients were clinically depressed compared with 4.3% controls ($P<0.001$, adjusted OR 2.40, 95% confidence interval (CI) 1.67–3.47). The highest adjusted OR for depression were found among patients with leg ulcers (OR 10.17, 95% CI 4.07–25.41), hand eczema (OR 4.00, 95% CI 2.01–7.97), atopic dermatitis (OR 3.27, 95% CI 1.61–6.62), psoriasis (OR 3.02, 95% CI 1.86–4.90), and infections of the skin (OR 2.65, 95% CI 1.39–5.06).

**Table 1. Characteristics of study population, *N* = 4,994**

| | Patients *N* = 3,635 *N* (%) | Controls *N* = 1,359 *N* (%) | *P*-value |
|---|---|---|---|
| *Countries* | | | |
| Belgium | 248 (6.8) | 131 (9.6) | — |
| Denmark | 256 (7.0) | 122 (9.0) | — |
| France | 114 (3.1) | 20 (1.5) | — |
| Germany | 278 (7.6) | 133 (9.8) | — |
| Hungary | 250 (6.9) | 134 (9.9) | — |
| Italy (two centers) | 499 (13.7) | 46 (3.4) | — |
| Netherlands | 213 (5.9) | — | — |
| Norway (two centers) | 527 (14.5) | 218 (16.0) | — |
| Poland | 250 (6.9) | 125 (9.2) | — |
| Russia | 248 (6.8) | 120 (8.8) | — |
| Spain | 249 (6.9) | 116 (8.5) | — |
| Turkey | 250 (6.9) | 109 (8.0) | — |
| UK | 253 (7.0) | 85 (6.3) | — |
| *Gender (MD = 17)* | | | |
| Females | 2,045 (56.5) | 903 (66.6) | <0.001 |
| Age years Mean SD (MD = 91) | 47.2 (SD = 17.9) | 41.1 (SD = 13.6) | <0.001 |
| Females | 46.0 (SD = 17.6) | 41.1 (SD = 13.3) | <0.001 |
| Males | 48.6 (SD = 18.2) | 41.1 (SD = 14.2) | <0.001 |
| *Marital status (MD = 322)* | | | |
| Single | 863 (26.0) | 362 (26.7) | <0.001 |
| Married/partner | 1,978 (59.6) | 840 (62.0) | — |
| Separated/divorced | 273 (8.2) | 119 (8.8) | — |
| Widowed | 203 (6.1) | 34 (2.5) | — |
| *Self-reported socioeconomic level (MD = 106)* | | | |
| Low | 644 (18.2) | 215 (15.9) | 0.183 |
| Middle | 2,589 (73.1) | 1,012 (75.1) | — |
| High | 307 (8.7) | 121 (9) | — |
| *Stressful life events during last 6 months (MD = 97)* | | | |
| Yes | 1,262 (35.6) | 412 (30.6) | <0.001 |
| *Physical co-morbidities*[1] *(MD = 479)* | | | |
| Yes | 993 (28.8) | 170 (16.0) | <0.001 |

Abbreviation: MD, missing data.
[1]Physical co-morbidities: any treated cardio-vascular, chronic respiratory, diabetes, or rheumatologic disease.

**Table 2. Distribution of common skin diseases among dermatological out-patients ($N = 3,635$) in 13 European countries**

| Diagnosis | Overall *N* ( %) | Countries *N* (%) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | BE *N* = 248 MD = 7 | DK *N* = 256 MD = 1 | FR *N* = 114 MD = 0 | DE *N* = 278 MD = 4 | HU *N* = 250 MD = 4 | IT *N* = 499 MD = 0 | NL *N* = 213 MD = 13 | NO *N* = 527 MD = 4 | PL *N* = 250 MD = 0 | RU *N* = 248 MD = 2 | ES *N* = 249 MD = 0 | TR *N* = 250 MD = 0 | UK *N* = 253 MD = 1 |
| Psoriasis | 626 (17.4) | 42 (17.4) | 41 (16.1) | 15 (13.2) | 27 (9.9) | 24 (9.8) | 82 (16.4) | 23 (11.5) | 128 (24.5) | 56 (22.4) | 67 (27.2) | 50 (20.1) | 25 (10.0) | 46 (18.3) |
| Non-melanoma skin cancer | 394 (10.9) | 34 (14.1) | 61 (23.9) | 7 (6.1) | 44 (161) | 2 (0.8) | 31 (6.2) | 48(24.0) | 102 (19.5) | 4 (1.6) | — | 24 (9.6) | 1 (0.4) | 36 (14.3) |
| Infections skin | 243 (6.8) | 17 (7.1) | 9 (3.5) | 6 (5.3) | 31 (11.3) | 16 (6.5) | 55 (11.0) | 10 (5.0) | 13 (2.5) | 18 (7.2) | 4 (1.6) | 18 (7.2) | 40 (16.0) | 6 (2.4) |
| Eczema | 229 (6.4) | 12 (5.0) | 16 (6.3) | 3 (2.6) | 23 (8.4) | 11 (4.5) | 23 (4.6) | 14 (7.0) | 18 (3.4) | 32 (12.8) | 20 (8.1) | 12 (4.8) | — | 45 (17.9) |
| Acne | 213 (5.9) | 11 (4.6) | 3 (1.2) | 2 (1.8) | 4 (1.5) | 3 (1.2) | 31 (6.2) | 3 (1.5) | 23 (4.4) | 6 (2.4) | 13 (5.3) | 9 (3.6) | 75 (30.0) | 30 (11.9) |
| Nevi | 177 (4.9) | 20 (8.3) | 2 (0.8) | 8 (7.0) | 10 (3.6) | 11 (4.5) | 34 (6.8) | 12 (6.0) | 16 (3.1) | 2 (0.8) | — | 42 (16.9) | — | 20 (7.9) |
| Atopic eczema | 162 (4.5) | 3 (1.2) | 6 (2.4) | 3 (2.6) | 11(4.0) | 22 (8.9) | 17 (3.4) | 3 (1.5) | 30 (5.7) | 30 (12.0) | 28 (11.4) | 2 (0.8) | 6 (2.4) | 1 (0.4) |
| Benign skin tumors | 152 (4.2) | 18 (7.5) | 4 (1.6) | 5 (4.4) | 10 (3.6) | 6 (2.4) | 35 (7.0) | 7 (3.5) | 12 (2.3) | 1 (0.4) | — | 37 (14.9) | 4 (1.6) | 13 (5.2) |
| Hand eczema | 143 (4.0) | 2 (0.8) | 16 (6.3) | 5 (4.4) | 16 (5.8) | 5 (2.0) | 17 (3.4) | 8 (4.0) | 20 (3.8) | 8 (3.2) | 16 (6.5) | — | 24 (9.6) | 6 (2.4) |
| Leg ulcers | 121 (3.4) | 1 (0.4) | 1 (0.4) | 4 (3.5) | 4 (1.5) | 79 (32.1) | 5 (1.0) | 8 (4.0) | 6 (1.1) | 7 (2.8) | 4 (1.6) | 1 (0.4) | — | 1 (0.4) |

Abbreviations: BE, Belgium; DE, Germany; DK, Denmark; ES, Spain; FR, France; HU, Hungary; IT, Italy (Rome and Padua); MD, missing data; NL, the Netherlands; NO, Norway (Oslo and Stavanger); PL, Poland; RU, Russia; TR, Turkey; UK, United Kingdom.

Table 4 gives data on anxiety in patients with common skin diseases. Overall, anxiety affected 17.2% of the patients compared with 11.1% of the controls ($P<0.001$, adjusted OR 2.18, 95% CI 1.68–2.82). The highest adjusted OR for anxiety disorders were found among patients with psoriasis (OR 2.91, 95% CI 2.01–4.21), leg ulcers (OR 2.80, 95% CI 1.18–6.64), hand eczema (OR 2.60, 95% CI 1.45–4.67), and acne (OR 2.53, 95% CI 1.40–4.58).

Suicidal ideation in common skin conditions is described in Table 5. Overall 12.7% of the dermatological patients reported suicidal ideation compared with 8.3% of the controls ($P<0.001$, adjusted OR 1.24, 95% CI 0.95–1.62). Only patients with psoriasis had a significant association with suicidal thoughts (OR 1.94, 95% CI 1.33–2.82). Of the patients reporting overall suicidal ideation, 53.6% reported that the suicidal thoughts were because of their skin condition: specifically 67.6% of patients with psoriasis and 68.0% of patients with atopic dermatitis reported suicidal ideation because of their skin.

## DISCUSSION

We found a significantly higher prevalence of clinical depression (10.1% vs. 4.3%), anxiety disorder (17.2% vs. 11.1%), and suicidal ideation (12.7% vs. 8.3%) among patients with common skin diseases compared with controls. These findings, from a wide geographical, cultural, and socio-economic base, have relevance for clinical services across Europe (Aguilar-Duran *et al.*, 2014) because of the high prevalence of skin diseases.

The reference values in our control group are in accordance with estimations of the European prevalence of mental disorders (Wittchen *et al.*, 2011). The co-occurrence of mental and dermatological problems has previously mostly been described in national single center studies. An Italian study of 2,579 dermatological patients showed an overall psychiatric morbidity of 25%, with a higher percentage of psychiatric cases in patients with skin infections, pruritic conditions, and alopecia (Picardi *et al.*, 2000). However, the General Health Questionnaire used in both studies does not specifically measure depression and anxiety, as it does not measure symptoms of distress. Therefore, the Hospital Anxiety and Depression Scale (HADS) seems more appropriate to use: this instrument has shown solid psychometric properties regarding factor analysis and internal consistency. Although there is a shared variance of 30% of the subscales of depression and anxiety, the sensitivity and specificity for the anxiety and depression subscales are high, which allows separation of anxiety disorder from depression (Mykletun *et al.*, 2001; Bjelland *et al.*, 2002; Picardi *et al.*, 2005; Breeman *et al.*, 2014).

The interpretation of previous published work is often made difficult because of a lack of prospective control group data, with many studies relying on population reference values. Our results are, however, compatible with a Danish study using the Beck Depression Inventory that reported a depression prevalence of 13% in dermatological patients compared with 5% among controls (Zachariae *et al.*, 2004).

Patients with leg ulcers had the highest rates of depression, and this association remained strong in the regression analysis.

**Table 3. Depression in patients with common skin diseases and controls in percentages and ORs (95% confidence interval) *N* = 4,994**

| Diagnosis | Depression clinical case HADS ⩾ 11% (*n*) | *P*-value | Crude OR[1] depression clinical case HADS > 11 | Adjusted OR[2] depression clinical case HADS > 11 |
|---|---|---|---|---|
| Psoriasis | 13.8 (84) | <0.001 | 3.23 (2.06–5.05) | 3.02 (1.86–4.90) |
| Non-melanoma skin cancer | 4.8 (18) | 0.729 | 1.21 (0.62–2.36) | 0.97 (0.41–2.32) |
| Infections skin | 8.9 (21) | 0.001 | 2.59 (1.40–4.76) | 2.65 (1.39–5.06) |
| Eczema | 8.0 (18) | 0.007 | 1.79 (0.89–3.59) | 1.68 (0.80–3.53) |
| Acne | 5.7 (12) | 0.311 | 1.53 (0.74–3.13) | 1.74 (0.73–4.17) |
| Nevi | 6.0 (11) | 0.215 | 2.05 (0.99–4.22) | 2.14 (1.01–4.53) |
| Atopic eczema | 10.1 (16) | <0.001 | 3.55 (1.82–6.92) | 3.27 (1.61–6.62) |
| Benign skin tumors | 4.8 (7) | 0.587 | 1.50 (0.69–3.65) | 1.43 (0.55–3.74) |
| Hand eczema | 15.1 (21) | <0.001 | 4.85 (2.59–9.10) | 4.00 (2.01–7.97) |
| Leg ulcers | 24.3 (28) | <0.001 | 11.23 (5.71–22.09) | 10.17 (4.07–25.41) |
| Dermatological out-patients overall | 10.1 (357) | <0.001 | 2.69 (1.88–3.84) | 2.40 (1.67–3.47) |
| Controls | 4.3 (58) | — | 1 | 1 |

Abbreviations: HADS, hospital anxiety and depression scale; MD, missing data; OR, odds ratio.
Missing data hospital anxiety depression scale-depression = 109 (patients = 102; controls = 7).
[1]Without participants with missing data for one or more of the predictors.
[2]Regression model for each disease separately, adjusting for gender, age, socio-economic status, stress, and co-morbidity.

**Table 4. Anxiety in patients with common skin diseases and controls in percentages and OR (95% confidence interval) *N* = 4,994**

| Diagnosis | Anxiety clinical case HADS > 11% (*N*) | *P*-value | Crude OR[1] anxiety clinical case HADS > 11 | Adjusted OR[2] anxiety clinical case HADS > 11 |
|---|---|---|---|---|
| Psoriasis | 22.7 (139) | <0.001 | 2.79 (2.02–3.85) | 2.91 (2.01–4.21) |
| Non-melanoma skin cancer | 8.0 (30) | 0.066 | 0.85 (0.52–1.90) | 1.17 (0.60–2.27) |
| Infections skin | 13.2 (31) | 0.179 | 1.59 (0.97–2.61) | 1.61 (0.93–2.78) |
| Eczema | 16.7 (37) | 0.013 | 1.78 (1.09–2.82) | 1.73 (1.01–2.93) |
| Acne | 15.1 (32) | 0.013 | 2.23 (1.41–3.52) | 2.53 (1.40–4.58) |
| Nevi | 11.2 (19) | 0.902 | 1.23 (0.69–2.20) | 1.32 (0.70–2.47) |
| Atopic eczema | 17.6 (28) | 0.006 | 2.29 (1.34–3.92) | 2.01 (1.10–3.68) |
| Benign skin tumors | 10.9 (16) | 0.753 | 1.44 (0.78–2.63) | 1.59 (0.80–3.15) |
| Hand eczema | 21.0 (29) | <0.001 | 2.93 (1.74–4.93) | 2.60 (1.45–4.67) |
| Leg ulcers | 17.5 (20) | 0.011 | 2.75 (1.39–5.44) | 2.80(1.18–6.64) |
| Dermatological out-patients overall | 17.2 (607) | <0.001 | 2.15 (1.69–2.75) | 2.18 (1.68–2.82) |
| Controls | 11.1 (150) | — | 1 | 1 |

Abbreviations: HADS, hospital anxiety and depression scale; MD, missing data; OR, odds ratio.
Missing data HADS-anxiety = 116 (patients = 107; controls = 9).
[1]Without participants with missing data for one or more of the predictors.
[2]Regression model for each disease separately, adjusting for gender, age, socio-economic status, stress, and co-morbidity.

These results confirm the psycho-social aspects of chronic leg ulcers: patients with chronic leg ulcers are often depressed and isolated (Moffatt *et al.*, 2009). We found an increased prevalence of depression among patients in the subgroup of eczema and atopic eczema and a higher odds ratio (OR) for depression in patients with atopic eczema. These findings correspond to those of Australian and Finish studies (Timonen *et al.*, 2003; Sanna *et al.*, 2014a). Hand eczema formed a separate subgroup of eczema that also showed an independent and high score for depression, again in concordance with previous studies (Niemeier *et al.*, 2002; Cvetkovski *et al.*, 2006; Boehm *et al.*, 2012).

**Table 5. Suicidal ideation in patients with common skin diseases and controls in percentages and OR (95% confidence interval) *N* = 4,994**

| Diagnosis | Suicidal ideation overall % (*N*) | *P*-value | Suicidal ideation because of skin disease (among those with suicidal ideation overall) %(*N*) | Suicidal ideation because of skin disease (in the whole sample) %(*N*) | Crude OR[1] suicidal ideation | Adjusted OR[2] suicidal ideation |
|---|---|---|---|---|---|---|
| Psoriasis | 17.3 (106) | <0.001 | 67.6 (71) | 11.6 (71) | 2.21 (1.59–3.07) | 1.94 (1.33–2.82) |
| Non-melanoma skin cancer | 6.9 (26) | 0.393 | 30.4 (7) | 1.9 (7) | 0.72 (0.42–1.24) | 1.60 (0.78–3.29) |
| Infections skin | 8.9 (21) | 0.760 | 33.3 (7) | 2.9 (7) | 0.69 (0.36–1.33) | 0.56 (0.28–1.11) |
| Eczema | 9.3 (21) | 0.623 | 61.9 (13) | 5.7 (13) | 0.93 (0.52–1.65) | 0.92 (0.50–1.70) |
| Acne | 12.3 (26) | 0.058 | 40.0 (10) | 4.7 (10) | 1.47 (0.90–2.39) | 1.01 (0.56–1.83) |
| Nevi | 12.9 (22) | 0.049 | 50.0 (11) | 6.4 (11) | 1.46 (0.84–2.55) | 1.52 (0.84–2.72) |
| Atopic eczema | 15.0 (25) | 0.002 | 68.0 (17) | 10.6 (17) | 2.03 (1.20–3.45) | 1.32 (0.75–2.33) |
| Benign skin tumors | 11.3 (17) | 0.208 | 52.9 (9) | 6.0 (9) | 1.16 (0.62–2.20) | 1.21 (0.61–2.41) |
| Hand eczema | 14.2 (20) | 0.020 | 45.0 (9) | 6.4 (9) | 1.49 (0.82–2.73) | 1.08 (0.57–2.08) |
| Leg ulcers | 17.8 (21) | <0.001 | 47.6 (10) | 8.4 (10) | 2.04 (1.03–4.04) | 1.27 (0.54–2.99) |
| Dermatological out-patients (all) | 12.7 (451) | <0.001 | 53.6 (238) | 6.7 (238) | 1.46 (1.13–1.88) | 1.24 (0.95–1.62) |
| Controls | 8.3 (88) | — | — | — | 1 | 1 |

Abbreviation: OR, odds ratio.
[1]Without participants with missing data for one or more of the predictors.
[2]Regression model for each disease separately, adjusting for gender, age, socio-economic status, stress, co-morbidities, and depression.

The highest rate of anxiety was reported in patients with psoriasis and hand eczema. The prevalence of depression among psoriasis patients and the significant OR of 3.02 are in accordance with a recent meta-analysis of 98 studies, showing that >10% of psoriasis patients have clinical depression (Dowlatshahi *et al.*, 2013). Our finding of anxiety in 17% of patients is higher compared with the findings of a global longitudinal study on psoriasis showing anxiety in 11% of patients (Kimball *et al.*, 2014) but in accordance with a recent study of psoriasis patients from Canada using the HADS (McDonough *et al.*, 2014). The rates of anxiety we found in patients with hand eczema were in agreement with a German study among 122 patients, also using the HADS, showing a 20% prevalence of anxiety (Boehm *et al.*, 2012).

By separating anxiety and depression some additional relevant observations have been made possible. Patients with acne have significantly more anxiety compared with the controls, but are not depressed, and patients have an OR>2 for clinical anxiety. Although a previous study showed a significant increased association between acne and mental distress, our findings are relevant (Halvorsen *et al.*, 2011). Suicidal thoughts were only significantly associated with psoriasis. This is in accordance with the study of Gupta *et al.*, (1993) among patients with psoriasis but in contrast to a recent study examining suicidal ideation in 907 men with physical illnesses, which did not find significant association with psoriasis in a model controlling for depression (Sanna *et al.*, 2014b). In our study, the increased rates of suicidal ideation for other skin conditions were not significant, suggesting that in our sample suicidal thoughts are secondary to other factors such as depression. It is possible that the ''yes'' or ''no'' response choice might have resulted in a higher recording of suicidal ideation. Nevertheless, the original aspect in this present study is that patients were specifically asked about suicidal ideation caused by skin symptoms.

This study has several strengths: first, the large European sample studied is a cross-section of dermatological out-patients. The breadth of diseases included and their widely differing psycho-social backgrounds provide robust overall data that compensate for some limitations by reflecting the reality of the populations served. Second, the presence of the control group enables us to compare the outcome variables with a reference population that is more appropriate than comparison to other patient groups. Finally, the high participation rate adds to the robustness of the study.

However, the study has several limitations. The study design did not allow face-to-face clinical interviews for confirmation of diagnosis of mental illness. However, the psychometric approach to evaluate depression used a self-administrated scale with strong psychometric properties.

There were differences in the prevalence of skin diseases from center to center. Although we planned to recruit only from clinics with general dermatology consultations, our data probably reflect some recruitment bias. There may have been bias in the selection of patients due to differences in the referral systems and organization of the clinics. Although all study centers have a special interest in psycho-dermatology, the small number of specific psycho-dermatological diagnoses ($n=22$) confirms that the sample came from general out-patients. By merging the whole data, we presume that the overall diagnosis distribution reflects that seen in any general out-patient clinic. This is supported by our prevalence data being comparable to a UK population survey on the

distribution of skin disease (Rea *et al.*, 1976). The study can be considered to be naturalistic and representative of dermatological out-patients in general, but the representativeness of the populations studied should be interpreted with care.

Length-biased sampling is potentially of concern for a study occurring over time, but it is suggested that the chronic non-lethal nature of the diseases studied limits that risk. The use of healthy, employed controls may introduce a bias; however, this is partly intended, as the control group reflects the desired state of health more closely than for example a group of other patients and because it allows more immediate comparison with other similar studies. For practical reasons the control group overall was smaller compared with the patient group, but this did not affect the results of the regression analysis. Furthermore, patients with severe mental disease were excluded, reducing the risk of bias. However, clinical data were not recorded and uncontrolled confounding factors such as disease severity, treatment, disease localization, or pruritus may have influenced patients' perception of their disease and hence the study results. The cross-sectional design of the study does not allow interpretation of the direction or causality of the associations between the skin diseases and the psychological outcomes.

This large European multicenter study demonstrates that adult patients with common skin diseases such as psoriasis, atopic dermatitis, hand eczema, and leg ulcers have significant psychological co-morbidities. These results identify a major additional burden of skin disease and have important clinical implications.

## MATERIALS AND METHODS

### Study design

This investigation was an observational cross-sectional multicenter study (for additional information see STROBE Supplementary Text in the JID homepage). Patients were recruited from dermatological out-patient clinics in 13 European countries from November 2011 to February 2013. Dermatology departments from the following centers participated: Erasmus Hospital, Brussels (Belgium), University of Copenhagen, Roskilde Hospital (Denmark), Brest University Hospital (France), Justus-Liebig University (Germany), University of Szeged (Hungary), University of Padua Medical School (Italy), Istituto Dermopatico dell'Immacolata, Rome (Italy), Radboud University Medical Center, Nijmegen (The Netherlands), Oslo University Hospital and Stavanger University Hospital (Norway), Wroclav Medical University, Wroclaw (Poland), Moscow Medical Academy IM Sechenov (Russia), Aragon Health Sciences Institute, Alcaniz Hospital (Spain), Sisli Etfal Teaching and Research Hospital, Istanbul (Turkey), and Cardiff University (UK). Two countries (Norway and Italy) had two centers of collection in different parts of the country.

### Ethics

The study protocol was approved by the Regional Committee for Medical Research Ethics in Norway REK 2011/1087. Local ethical approval was obtained where necessary. The study was conducted in accordance with the Declaration of Helsinki.

### Settings

At each dermatological out-patient clinic, consecutive patients were invited to participate in the study on one or more random days until 250 were reached. The inclusion criteria were age >18 years, being able to read and write the local language, and not suffering from severe psychosis, to reflect the majority of patients and avoid any overestimation of any possible co-occurrence between mental and skin disease. Each participant completed a questionnaire and gave it to the consultant before being examined clinically.

Each patient was examined by a dermatologist who recorded the diagnosis; if required a secondary diagnosis was recorded. The presence of other physical conditions was recorded: cardio-vascular disease, chronic respiratory disease, diabetes, and rheumatologic disease. If there were doubts as to whether a skin disease was present (eg, no diagnosis, no flares, and no itch) the patients were not included in the sample.

In each center, a control group of at least 125 subjects were recruited by advertisement from among hospital employees at the same institution but not from the same department. Only those willing to participate were included. Employees with a skin condition were excluded. The employees were informed about the study and invited to answer the questionnaire after giving written consent. The subjects were not examined. Information on treated co-morbidities was self-reported. All participants were informed and gave signed consent.

### Questionnaires

The first part of the questionnaire recorded socio-demographic variables including self-reported socio-economic status. Ethnicity was self-assigned by each participant referring to their own country of birth. Stress was assessed with the item ''Have you had any stressful life events during the last 6 months?'' with a possible answer of ''yes'' or ''no''.

Symptoms of depression and anxiety, the main outcome variables, were assessed with the HADS, a well-validated instrument showing good psychometric properties, to assess severity and presence of anxiety disorders and depression in somatic, psychiatric, and primary care patients, as well as in the general population (Zigmond and Snaith, 1983; Mykletun *et al.*, 2001; Bjelland *et al.*, 2002). HADS includes seven items assessing anxiety and seven for depression, each with four possible answers. For each dimension of anxiety and depression a score from 0 to 7 is considered a normal case, from 8 to 10 a borderline case, and from 11 to 21 a case in need of further examination or treatment. This instrument was used in the validated translations relevant to the study countries.

To assess suicidal ideation, we included the item ''Have you ever thought of committing suicide?'' with possible answers ''yes'' or ''no'': we were not able to identify a validated item on suicidal ideation. An additional question was given to the patient group: ''Have you ever thought of committing suicide because of your skin?'' with an item on frequency when the answer was yes.

### Statistical analysis

The statistical power was calculated on the basis of the prevalence of depression in the general population estimated as 9% and the expected prevalence in the dermatological population being higher (Hinz and Brahler, 2011; Breeman *et al.*, 2014). However, as our cases were nonselected out-patients with several skin conditions at various degrees of severity, we expected to find a lower prevalence. To identify a difference with a power of 0.80 and alpha = 0.05 between a prevalence of depression of 9% in controls and 11% in cases, using a one-sided test, 3,500 cases and 1,300 controls were

needed (about 233 cases and 87 controls in each center). The data were entered in an SPSS or Excel database at each site, after completion of data collection (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY). Ten sets of questionnaires from each center were sent to the Statistical Center (Institute of Medical Psychology, University of Giessen, Germany, not a recruiting center) to ensure that the data had been entered in a standardized way. The final data were merged in a single file and checked and cleaned. The diagnoses given in different European languages were translated by the dermatologists from the study team to diagnoses from the International Classification of Disease version 10. If needed, national centers were consulted.

The dermatological diagnoses were organized into 26 categories adapted from the Lambeth study (Rea *et al.*, 1976). Data were used only if the diagnostic group included at least 100 patients, 10 diagnoses fulfilled this criterion, and hence we performed the analysis on the 10 most prevalent diagnostic categories from the total sample. The diagnostic categories with $<100$ patients included a large range of dermatological conditions; results are not shown.

SPSS version 22 software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0) was used to analyze the data. To characterize the study population, we report numbers, percentage, or mean values with standard deviation. To compare the patients and the controls, we used the *t*-test for continuous variables and the $\chi^2$-test for dichotomous or categorical variables. We describe the prevalence of depression, anxiety, and suicidal ideation with percentages and numbers.

To compare the prevalence between the disease groups and the controls, we used the $\chi^2$-test for dichotomous variables. Multivariate logistic regression models were tested to study the associations between main outcome variables (depression, anxiety, and suicidal ideation) and groups (patients and controls). The regression models were calculated for each disease separately, adjusting for gender, age, socio-economic status, stress, and co-morbidity.

The ORs were calculated from the estimated regression coefficients B from the logistic regressions. The exponential of the coefficient gives the OR. In the first step, we calculated the crude ORs and in the second adjusted ORs simultaneously controlling for potential confounding factors (gender, age, socio-economic status, perceived stress, co-morbidities, depression (only for the logistic regression for suicidal ideation) with a 95% CI.

In the regression models the Netherlands, France, and Italy centers were excluded because no controls were recruited at these centers. Other analyses were performed with the complete data set. Cases with missing data for single variables were excluded from the analysis when necessary.

The differences in the percentage of diagnoses between the centers represent the prevalence of diagnoses in different countries. These differences were accepted as reflecting the real life situation in different populations of dermatological out-patients: for instance, Turkey has more acne patients, as a result of the younger average age of the population in Turkey.

## CONFLICT OF INTEREST

The authors state no conflict of interest.

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## Disclaimer

All authors are members of the European Society for Dermatology and Psychiatry.

## SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/jid

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